X-Shaped Macular Dystrophy with Flavimaculatus Flecks

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Abstract: Two families showed a retinal pigment epithelial dystrophy characterized by an X-shaped yellowish macular lesion and numerous flavimaculatus retinal flecks. Nine members were variously affected. The condition was bilateral, had a dominant inheritance and started in middle age with a slow-developing macular lesion. Visual functions were often minimally disturbed for 2 or 3 decades. The flavimaculatus flecks which differed in number appeared only as secondary phenomena yet increased in number and size. At the onset of the disease, the ERG and EOG as well as colour vision were normal and became altered only in the course of a very slow process.

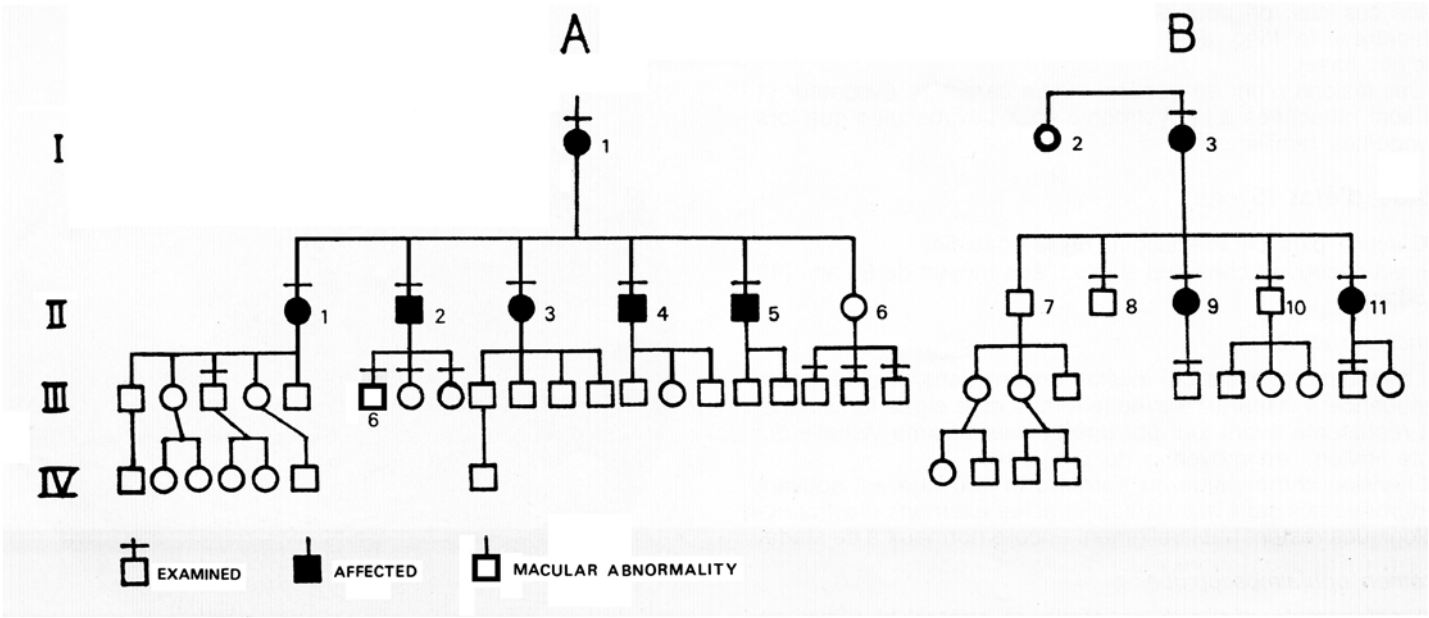

Fig.1: Pedigree of families A and B

Introduction:

In the early sixties, Franceschetti [2] introduced the term fundus flavimaculatus in order to discriminate, from the r est of flecked-retina abnormalities (table 1), a specific aspect of the eyeground characterized by numerous, pisciform, deep, yellowish retinal flecks with fuzzy borders. His new entity assumed two major forms: the first one did not entail macular involvement, was non-evolutive and was said to be the 'pure', the other one was characterized by macular involvement [2].

Following the claim of Irvine and Wergeland in 1972 [6], in 1975, we [3, 13] claimed that Stargardt's disease and fundus flavimaculatus were one and the same, which conclusion has since been agreed l.;lpon by all the authors. Indeed, we had never found a form of fundus

flavimaculatus which was really pure, ~onevolutive and not associated with macular involvement; then, we concluded that only the form with macular involvement did exist. Therefore, fundus flavimaculatus was only a clinical form of Stargardt's disease.

In 1988, because of the extremely slow evolution of the late form of fundus flavimaculatus and its specific clinical aspect, we considered the possibility of there being a different gene, which implied that there existed an affection distinct from Stargardt's disease [15]. The discovery, within two families, of 9 patients affected by a late form of the condition at different stages of its evolution enabled us to establish its individual, specific nature.

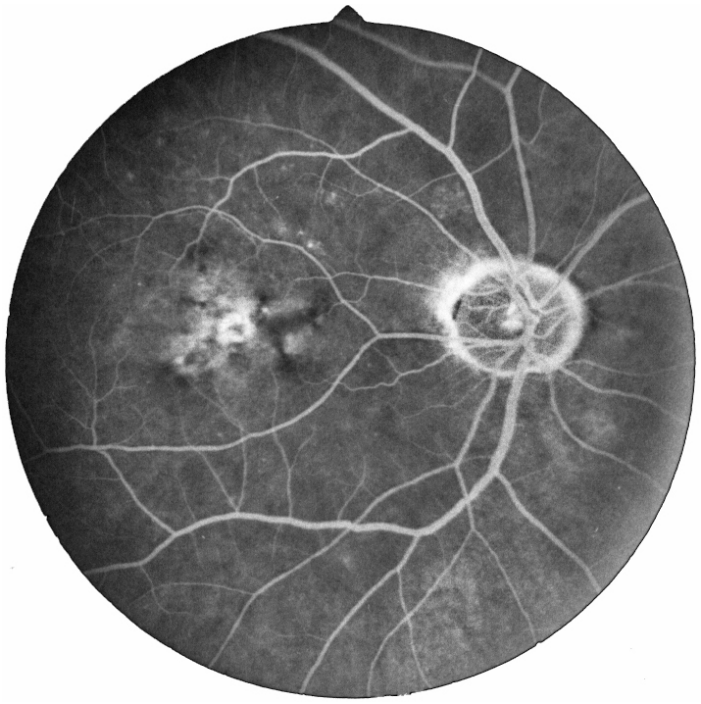

Fig. 2: Case 1. Angiogram of the right macula with X-shaped foveolar lesion with hypofluorescence and a small area of parafoveolar atrophy. Disturbances of the pigment epithelium in the region of the upper temporal vessels.

Fig. 3: Case 2. Photograph of the right macula with X-shaped yellowish foveolar lesion and numerous peripheral flavimaculatus flecks.

Subject and Methods :

Out of a population of 4 million inhabitants in the north of France and within 15 years of study, we discovered 215 patients who were affected by Stargardt's disease, and we discriminated them according to table 2.

Out of those patients, 108 are affected by a flavimaculatus form of the disease and in 17 of them, it is a late form. Among those 17 later cases of fundus flavimaculatus, 8 appear to be autosomal recessive or sporadic, and 9 are autosomal dominant. The 9 dominant cases are the subjects of this study (table 3); they belong to two pedigrees and formed a perfectly homogeneous group whose heredity cannot be questioned (fig. 1). Only 7 of the 9 patients studied unterwent function tests in Lille (Regional Hospital). The files of the other 2 patients were handed over to us by their ophthalmologists. The first examination enabled us to discover that 3 of 7 patients examined in Lille were affected by extensive flavimaculatus lesions which we first labelled as late, slow-developing forms of Stargardt's disease; initially, the other 4 patients showed reticular macular or atrophic lesions which suggested a network-like dystrophy. Four of those 7 patients were followed over a period of 10 years.

Table 1: Flecked-retina hereditary diseases

Drusen	
Scattered with or without macular involvement	AD
Radial pattern	AD
Hutchinson-Tay central guttate choroiditis	AD
Malattia leventina	AD
Mulibrey nanism syndrome	AR
Retinitis punctata albescens	
Retinitis punctata albescens, isolated	AR
Fundus albipunctatus (Lauber's disease)	AR
Bietti's corneal dystrophy	AR|XL
Hyperoxaluria	AR
De Toni-Fanconi syndrome	AR
Cystic fibrosis syndrome	AR
Scattered or macular vitelline material	
Adult foveomacular dystrophy	AD
Fundus flavimaculatus	AD/AR
Best's dystrophy (vitelliform or scattered form)	AD
Pseudo-vitelliform dystrophies	AD
Pattern dystrophies	AD
Macular affections with macular or perimacular flecks	
Olivopontocerebellar degeneration retinopathy	AD
Slowly progressive macular dystrophy	AD
Myotonic dystrophy syndrome (Steinert's syndrome)	AD
Von Gierke's disease	AR
Rubinstein-Taybi disease	AR
Sjogren-Larsson syndrome	AR
Stargardt's disease without fundus flavimaculatus .	AR/AD
Alport's syndrome	AD/XL
Lignac-Fanconi syndrome (cystinosis syndrome)	AR
Kjellin's syndrome	AR
Rare affections with retinal flecks characterized by fuzzy borders	
Primitive nephropathic amyloidosis	AD/AR
Hallervorden-Spatz syndrome	AR
Leber's tapetoretinal dystrophy (rare flecked form)	AR
Kandori's syndrome (equatorial flecks)	AR?
X-linked juvenile retinoschisis (rare flecked form)	XL

AD = Autosomal dominant; AR = autosomal recessive; XL = X-linked

Case Reports :

Family A

Case 1 (I-1). A 74-year-old woman, the mother of the 5 patients reported below, was referred to us in 1984 in order to check a senile macular degeneration with metamorphopsias in the right eye. Her visual acuity was 20/100 in the right eye and 20/30 in the left eye. Colour vision, tested with the lOO-HUE test, was found slightly altered. The right eye showed an atrophic yellow-red foveola with X-shaped yellowish beams radiating from it. In the left eye, a yellowish substance entirely covered the foveola and extended to the macular area, thus assuming the pattern of a five-branched star with a metallic sheen. Several yellowish flecks could be seen on the posterior pole and at the level of the upper and lower temporal vessels. On angiography, the same aspect could be seen in both eyes (fig. 2): the X-shaped macular branches looked dark, but their outlines showed a 'window defect' which suggested an alteration of the pigment epithelium. In addition, in the left eye, there existed an area of macular pigment involvement and several flavimaculatus fluorescent lesions in the temporal
region. At the time, no genetic investigation was performed, and no connection with the children's own conditions was established. By 1988, an ophthalmoscopic examination showed a similar aspect in both eyes. Visual acuity was 20/125 in the right eye and 20/50 in the left eye.

Table 2: Stargardt's disease and fundus flavimaculatus (215 patients).

	Cases n	%
Recessive or sporadic Stargardt's disease without flavimaculatus	103	48
Dominant Stargardt's disease without flavimaculatus flecks	4	2
Recessive or sporadic flavimaculatus Stargardt's disease	72	34
Dominant flavimaculatus Stargardt's disease	19	9
Late dominant fundus flavimaculatus	9	4
Late recessive or late sporadic fundus flavimaculatus	8	3

Case 2 (II-1). In 1985, a 49-year-old woman consulted us due to a conjunctivitis. Her visual acuity was excellent, being 20/20 in both eyes. An ophthalmoscopic examination revealed numerous, irregular, dirty yellow flecks, a certain number of which was situated in the macular region and which formed an area characterized by irregular borders (fig. 3).
The patient mentioned that her mother had similar visual complaints. The ERG and VER were normal. The EOG was normal in the right eye yet somewhat weak in the left one (light/dark ratio of 1.87 and 1.63). On fluorescein angiography (fig. 4), the aspect of the eyeground was similar to that of her brother (case 3) as reported below; there were many flavimaculatus flecks extending from the perimacular region to the periphery.

Fig. 4: Case 2. Fluorescein angiogram of the right eye. Macular masking effect of vitelline material with varying fluorescence of the flavimaculatus regions.

Fig. 5: Case 3. Photograph of the left eye with yellowish macular lesion and flavimaculatus flecks.

Case 3 (II-2). A 41-year-old man, whose condition was detected during a routine check-up at work, was referred to us in 1978. His visual acuity was *20/20* in both
eyes; the lOO-HUE test gave normal results. The patient did not complain of any specific troubles, but ophthalmoscopic examination revealed numerous yellowish lesions (fig. 5). The lesions were strongly suggestive of fundus flavimaculatus, but the macular aspect was far from being typical. At the level of the macula, in both right and left eyes, several X}shaped yellowish flecks looked slightly thicker than the neighbouring flavimaculatus flecks and were suggestive of a vitelline material with fairly clear borders and standing out against an unaltered retina. On fluorescein angiography those macular flecks had a

masking effect with fluorescent outlines (fig. 6). The ERG, EOG and VER were normal. Profile perimetry showed a slightly depressed macular peak. An examination performed in 1979 showed increased macular and peripheral lesions although visual acuity was not diminished. In 1988, it was no longer so: visual acuity fell to *20/40* in the right eye and *20/30* in the left one. The visual field presented a perifoveolate scotoma in the right eye and diminished liminal thresholds in both right and left eyes. The ERG showed a global alteration of the photopic and scotopic values. On angiography, the aggravated atrophy of the pigment epithelium was confirmed, both around the macular lesion and the flavimaculatus flecks (fig. 7, 8). At that time, after examining his 3 children, it was discovered that one of his sons (III-6) displayed a discrete pigment epithelial cluster in the right macula.

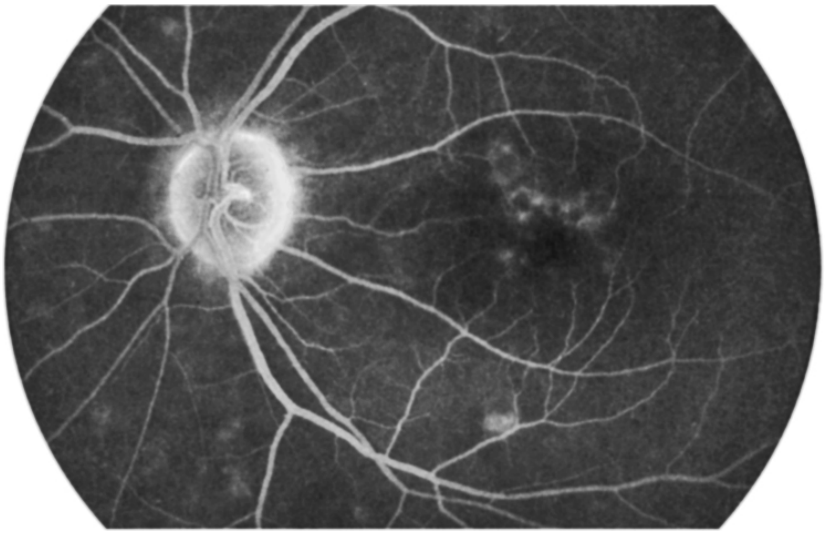

Fig. 6: Case 3. Angiogram of the left eye with macular masking effect and hypofluorescence of the lesion.

Fig. 7: Case 3. Same eye as in figure 5 and 6, 10 years later. Extension of the macular and flavimaculatus lesions.

Case 4 (II-3). In 1978, a 40-year-old woman consulted Dr. Montauffier in Toulon, because she was suffering from a slightly diminished visual acuity at near. Her visual acuity was *20/20* in both eyes. There existed a slight presbyopia, but in the right fundus, the ophthalmologist discovered a macular and paramacular lesion which prompted him to perform a fluorescein angiography whose aspect was absolutely similar to that of her
brother (II-2).

Case 5 (II-4). A 43-year-old man consulted due to a diminished visual acuity in the right eye which was *20/40* uncorrected and slight metamorphopsias. His corrected visual acuity was *20/20* in both eyes. The eyeground showed very discrete degenerative macular lesions in both eyes with a discrete paramacular pigmentation in the right eye. Small flavimaculatus flecks could be observed along the upper temporal vessels in the right and
left eyes. On fluorescein angiography, on the underside of the ophthalmoscopic lesions a discrete atrophy of the macular pigment epithelium was detected in the right eye: it was expressed by a small window defect area with a dark centre (fig. 9); along the upper temporal vessels, the flavimaculatus flecks showed a discrete window defect.

Case 6 (II-5). In 1982, a 40-year-old man consulted us due to two peripheral retinal haemorrhages in the right eye and a bilateral macular dystrophy. His visual acuity was 20/25 in both

eyes. On fundus examination a yellowish macular lesion was visible together with a few flavimaculatus flecks in the posterior pole and under the temporal vessels in both eyes. On fluorescein angiography, we detected a discrete macular window defect on the underside of the yellowish lesions and a window defect at the level of the flavimaculatus flecks.

Fig. 8: Case 3. The macular masking effect is particularly evident.

Fig. 9: Case 5. Locally limited atrophy of macular pigment epithelium and slight flavimaculatus lesions under upper temporal vessels.

Family B

Case 7 (II-11). In 1978, a 39-year-old woman, the sister of the patient below and the daughter of patient 9, had been affected for a year with small metamorphopsia with a bilateral X-shaped yellowish macular dystrophy. Visual acuity was 20/20 in the right eye and 20/25 in the left one. The ERG and EOG were normal. On fluorescein angiography, a complete window defect of the macula caused by the atrophy of the pigment epithelium was visible; the X-shaped lesion had a locally masking effect of that window defect. Tiny yellowish flecks could be seen along the upper and lower temporal vessels. The diagnosis of an atypical form of Deutman's butterfly dystrophy was established. The patient was examined again in 1988; visual acuity was weak 20/20 in the right eye and 20/25 in the left one. Slight metamorphopsias still persisted; the X-shaped pattern of the yellowish macular beams had extended; numerous pisciform flavimaculatus flecks had appeared and were covering the whole surface of both retinas, from the posterior pole to the periphery (fig. 10, 11). An area devoid of pigmentation was also visible in the periphery. The somewhat weak ERG prov~ded normal photopic and scotopic values. The EOG ratio was slighty altered, but its upper limits remained acceptable. On angiography, the foveola masked by an X-shaped vitelline material showed a sharply defined hyperfluorescence along the edges of the vitelline material.

Case 8 (II-9). In 1978, a 44-year-old woman was referred to us by her ophthalmologist due to an Xshaped macular dystrophy. Her visual acuity was 20/25 in the right eye and 20/20 in the left one. The patient mentioned a slight, slowly disappearing metamorphopsia. The macular lesions which were extremely discrete on direct ophthalmologic examination, were clearly visible under anerythre light.

The lesions were identical to those of her sister (II-11) but more discrete; several yellowish flecks looking like atypical drusen could be detected . along .the upp~r and lower temporal vessels (fig. 12). By 1988, the lesions had not extended, but the macular vitelline material had taken a greyish aspect. Visual acuity had not diminished.

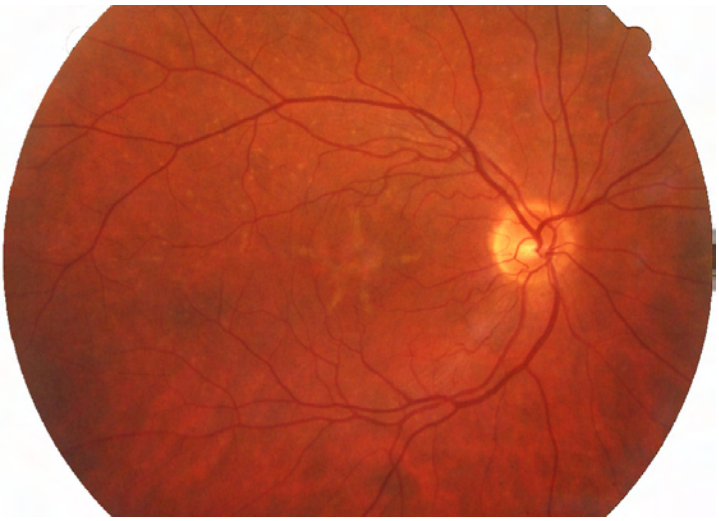

Fig. 10: Case 7. Yellowish macular lesion as seen on aneryhtre light.

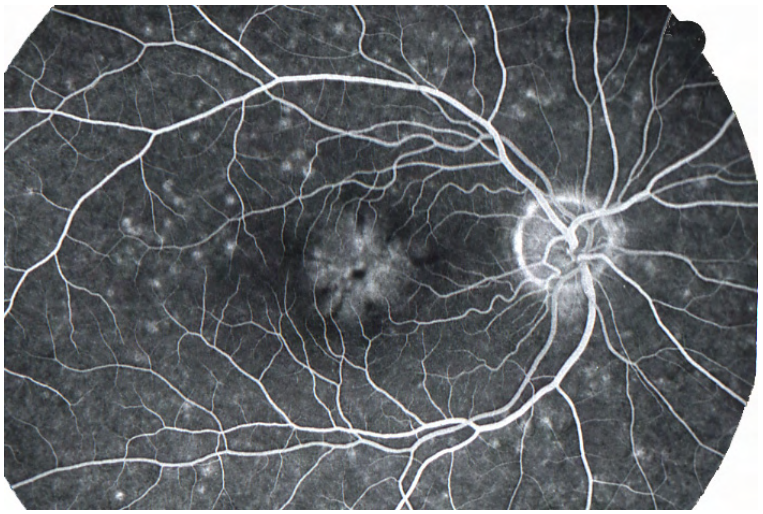

Fig. 1l: Case 7. On angiography, the masking effect vitelline material is made evident together with slight flavimaculatus flecks.

Case 9 (I-3). A 76-year-old woman was examined, due to a bilateral senile cataract. Her visual acuity was *20/70* in both eyes. Surgery was postponed, because cataract was not the main reason for her diminished visual acuity: indeed, in the eyeground, a network-like atrophic macular alteration could be detected, and in the periphery, there existed a few yellowish flecks similar to drusen. In the absence of photographs and angiograms, it was not possible to establish an absolutely unquestionable link between the patient's condition and that of her sister. Aged 84, the latter was being treated somewhere around Paris, because she had bilateral degenerative atrophic lesions. Her visual problems started in 1976. In 1988, visual acuity was impaired, and, in addition, the patient was affected, like her sister, by a cataract. Her macular lesions were then suggestive of an age-related qegeneration.

Results :

After examining our patients and studying the results, we can distinguish three stages in the evolution of this condition, depending on the onset of the disease and ophthalmoscopic aspect.

Onset Stage

The complaint is discovered after middle age (at 50 on the average). The first functional signs often involve a central, generally unilateral, metamorphopsia. Visual acuity remains normal. The discovery of retinal lesions is made during routine fundus examination. The macular lesion which consists of a yellowish vitelline material, assumes the shape of a
multi-branched cross whose branches (4 or 5 in number usually) meet in the middle of the foveola. Very discrete on ophthalmoscopy, the lesion is clearly visible under aneryhtre light (fig. 3). In a certain number of cases, yellowish flecks may already be detected around the main temporo~vascular vessels. On angi?graphy, the cross-shaped yellowish material causes
a discrete masking effect which is associated with a discrete window defect in the macular region (fig. 4). That window defect is the expression of a slight alteration of the pigment epithelium which seems to

occupy the whole macular area and to be masked by the vitelline material. On fluorescein angiography, the yellowish peripheral flecks have the same aspect
as in a fundus flavimaculatus, with a window defect which is characterized by irregular outlines and which is all the more visible in earlier flecks. It is worth noting that, in none of those cases, a Bonnin's silent choroid was detected, even before the occurrence of flavimaculatus flecks. Colour vision and the ERG are normal as well as the EOG whose values remain normal thought it may sometimes provide borderline ratios.

Table 3 Clinical and biological data in 9 patients and evolution

Patient N	I-1	II-1	II-2	II-3	II-4	II-5	II-11	II-9	1-3
Sex	F	F	M	F	M	M	F	F	F
Year of birth	1912	1935	1937	1938	1940	1942	1935	1940	1912
Age of discovery	72	49	41	40	43	40	39	44	72
Onset form.	X-FF	X-FF	X-FF	X-FF	A-FF	A-FF	X-FF	X-FF	A-FF
Corrected visual acuity									
First examination									
RE	20/100	20/20	20/20	20-20	20/40	20/25	20/20	20/25	20/70
LE	20/30	20/20	20-20	20/20	20/20	20/25	20/25	20/20	20/70
In 1988									
RE	20/125	20/20	20/40	20/20		20/25	20/20	20/25	20/70
LE	20/50	20/20	20/30	20/20		20/25	20/25	20/20	20/70
Metamorphopsia	++		++				++	+	
Colour vision	N		N	N			N	N	N
X-shape	+	+	+	+			+	+	
Macula, atrophic					+	+			
Flavimaculatus flecks									
Numerous		+	+	+					
Scarce	+				+	+	+	+	+
Onset ERG									
Photopic									
RE		N	N				N		
LE		N	N				N		
Scotopic									
RE		N	N				N		
LE		N	N				N		
Onset EOG									
RE		N	N				N		
LE		N	N				N		
Ratio									
RE		1,87	2,30				1,71		
LE		1,63	1,88				1,75		

X-FF=X-shaped macular dystrophy with fundusflavimaculatus; A-FF= atrophic macular dystrophy with fundus flavimaculatus; RE= right eye; LE= left eye; N= normal.

Development Stage

At that stage, the metamorphopsias may fade or disappear, and visual acuity may fall several points. The ophthalmoscopic aspect and especially the anerythre aspect are characteristic: they reveal an extension of the X-shaped macular lesion and an increase in the number and size of flavimaculatus flecks (fig. 4, 5). Usually, the results of electrophysiological examinations still give normal results at that stage.

Later Stage

Visual acuity falls several points further down, but, on the whole, remains fairly good (20/100-20/40), the minimum acuity being 20/125 in a 76-year-old patient (case 1). On fundus examination, it is possible to detect an acceleration of the process leading to the atrophy of the pigment epithelium, together with, sometimes, a more or less well-centred areolar atrophy (fig. 2). The yellowish macular material tends to expand then to disappear, with the X-shaped cross losing some of its branches and the peripheral flecks increasing in number. On fluorescein angiography, the macular window defect has extended but still

remains limited to the macular area. At that stage, an alteration of the colour vision may be detected, without there being a specific axis of alteration. The ERG and EOG may also be altered.

If this description bears only on the common features of the disease, a thorough examination of all the members of the family may reveal minor forms of the disease which do not entail any functional disturbances. Some asymptomatic cases are characterized by a macular lesion limited to a few yellowish perifoveolar flecks which correspond to the branches of the cross to be formed (fig. 9). In such cases, on fluorescein angiography, a pentagon image appears clearly: it corresponds to the diameter of the foveola, has a fluorescent periphery, and its centre masks the dye (cases 5 and 6). Flavimaculatus flecks may also be extremely varied in number and size; they may be hardly existent as in case 1 or look a constellation as in some other cases (cases 2, 3, 7).

In the elderly patient, if there is no family history of the disease, the diagnosis of the condition is hardly ever established, because "the ophthalmoscopic and fluorographic characteristics of the disease have disappeared.

If we study the figures given in table 2, the condition (both dominant and isolated forms of the disease) appears in lout of 6 cases of flavimaculatus Stargardt's disease, which corresponds to a frequency of 1170000, taking into account the frequency of the flavimaculatus Stargardt's disease in our region [15].

A close study of our pedigrees does not rule out a pseudo-dominance, but since the condition appears only after the age of 50, it is difficult to find more than two affected generations. Also, within those two families and assuming that there exists a dominant inheritance, beside the number of affected patients who are really affected, the other members of the family are not prompted into having their eyes tested in hospital and into having further research made.

Fig. 12: Case 8. X-shaped macular lesion under formation.

Discussion

Many other conditions are characterized by yellowish retinal flecks (table 1), yet, in most of them, the flecks are quite different and cannot be mistaken for flavimaculatus flecks.

The X-shaped flavimaculatus macular dystrophy must be distinguished from the typical forms of Stargardt's disease. In the occurrence of flavimaculatus Stargardt's disease, within 10 years from the onset of the disease, visual acuity sharply falls to *20/125*, and the macula seems to be functionally destroyed. In

our patients, it takes 2 or 3 decades for the vitelline material to appear and 2 or 3 more decades for, visual acuity to fall significantly. In Stargardt's disease, a dyschromatopsia is an early, classical feature, yet it can never be found in our patients. In our patients the slight metamorphopsias may be the first conspicuous symptom, yet they can never be found in the early stages of Stargardt's disease. Whereas in Stargardt's disease, the ERG which is not noticeably altered at first becomes drastically altered within less than 4 or 5 years, especially in the red photopic values. In our patients, the ERG and EOG retinal function tests give minimally altered values even 10 years after the onset of the disease. On angiography, the bull's eye lesion is one of the characteristics of Stargardt's disease; in some advanced forms of the disease, it is replaced by an overall macular masking defect. In our patients, there is no such bull's eye lesion but a macular masking effect caused by a vitelline material and a very slow-developing, deep-seated macular alteration.

In everyday pathology, most cases are isolated and atypical; depending on the importance given to one trait among others, one may be led to classify ill-defined disturbances into the category of well-known, classical diseases, on the grounds that they are borderline or intermediate forms. We have read through the medical literature, looking for cases similar to ours. We took into account, the three criteria specific to the condition which we were studying: visible flavimaculatus flecks, age over 40 and well-preserved visual acuity. Several cases then seemed to fall into the category defined by us: case 18, a 45-year-old woman, and case 20, a 50-year old man, in Klien and Krill [7]; case 3, a 50-year old man, and case 5, a 45-year-old woman, in Krill and Klien [9]; case 18, a 53year old man, in Klein et al. [8]; a 52-year old woman in Leveille et al. [10]; a 66-year old woman, described in figure 16-5, in Newsome and Blacharski [11].

Since the condition has a dominant inheritance, is expressed by different forms and takes 50 years to develop, it is not surprising if the diagnosis can only be applied to one generation and if most observations are considered as sporadic, as we discovered in half the cases studied (table 2).

In 1974, Gass [4] described the foveolomacular dystrophy of the pigment epithelium in the adult as being a disease very similar to that of our patients, since it had a late occurrence and since, as in most of our patients, it was characterized by a macular vitelline material which was most often rounded rather than star-shaped [12]. But, in that disease, there may exist a few tiny yellow flecks (2 or 3) in the paracentral area, and we may wonder whether the forms of the disease, involving a few discrete flavimaculatus flecks, do not in fact correspond to the onset stage of a slightly atypical form of the condition affecting our patients. The 3 patients (fig. 5-9, p.253, photograph A1) presented by Gass in 1987 [5], as being affected by a slightly atypical form, probably involving a network-like dystrophy, as in a fundus flavimaculatus, associated with vitelliform lesions do seem to belong to the same group as our own group of 9 patients.

In 1977, Singerman et al. [14] described a family affected by a dominant slowly developing macular dystrophy which corresponded exactly to an X-shaped flavimaculatus macular dystrophy. The condition was dominant and appeared late in life (after the age of 50). 23 members presented macular alterations to various different extents; 3 patients (cases 3, 4 and 6) had an X-shaped macular dystrophy, flavimaculatus flecks, a rather good visual acuity, a normal EOG and slightly altered ERG. The other members were affected either by a starshaped macular vitelline lesion (cases 1, 5 and 8), or by a senile or atrophic macular degeneration. However, no connection was established between the late forms of fundus flavimaculatus and the possibility that the late forms were a new, different entity.

From a nosological point of view, it is crucial to establish the identity of the X-shaped flavimaculatus macular dystrophy so as to differentiate it (1) from Stargardt's disease, because the above condition implies a much better prognosis, (2) from pattern dystrophies which neither involve a star-shaped development of the central lesion nor flavimaculatus flecks, and (3) from Gass's foveomacular dystrophy whose occurrence is more frequent and whose development remains limited to the macular area.

In short, the emergence of that late form of macular dystrophy should make it possible to achieve a better knowledge of late, atypical macular dystrophies which are too often classified as 'senile' or 'vascular'.

Conclusion

The term fundus flavimaculatus which was coined to describe a specific aspect of a flecked retina, is no longer the exclusive synonym for Stargardt's disease. It corresponds to a specific suffering of the pigment epithelium which is expressed by the presence of deep-seated, network- like retinal deposits of lipofuscin, a yellowish pigment [1]. That dystrophy now corresponds to two very different conditions:
- The first one is severe, involves an early functional alteration of the cones and a rapid alteration of the macular function with the destruction of the macular pigment epithelium. It corresponds to Stargardt's disease and usually occurs at an early age.
- The other one, characterized by an extremely slow development, corresponds to a global retinal dystrophy characterized by the occurrence of an X-shaped macular vitelline material, numerous peripheral flavimaculatus flecks and by a long-retained visual acuity.

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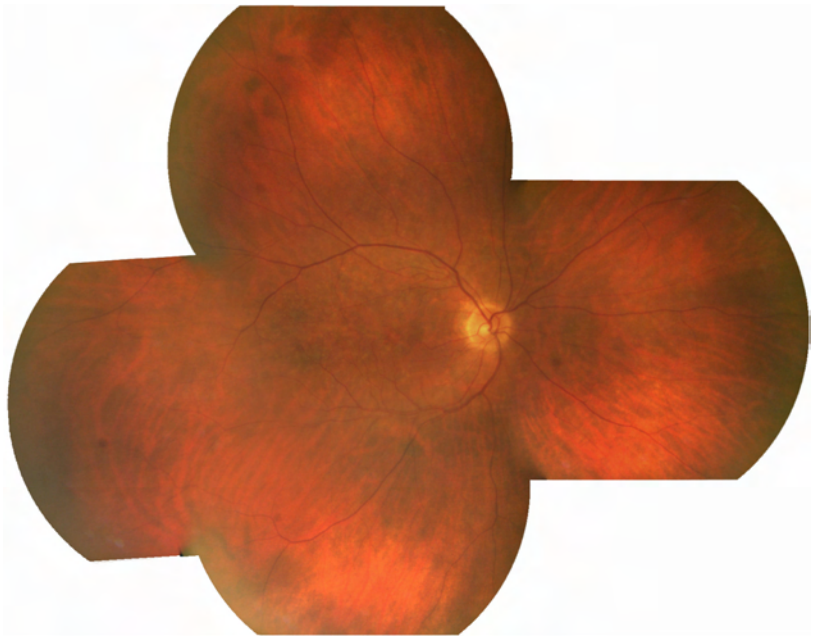
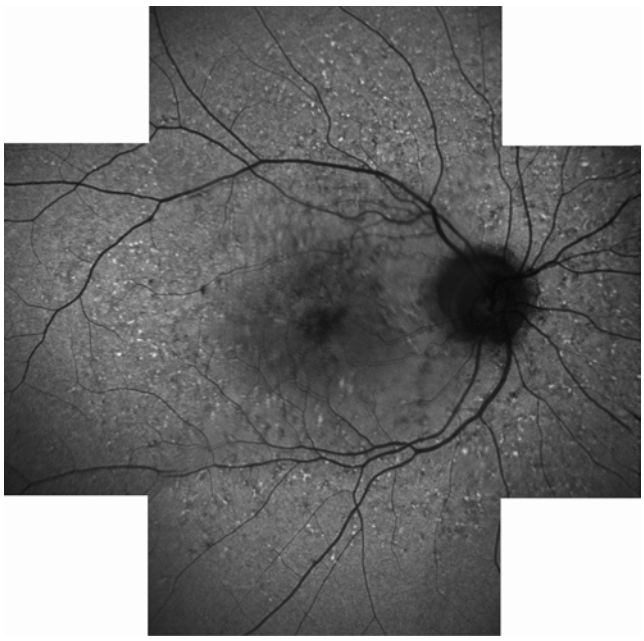
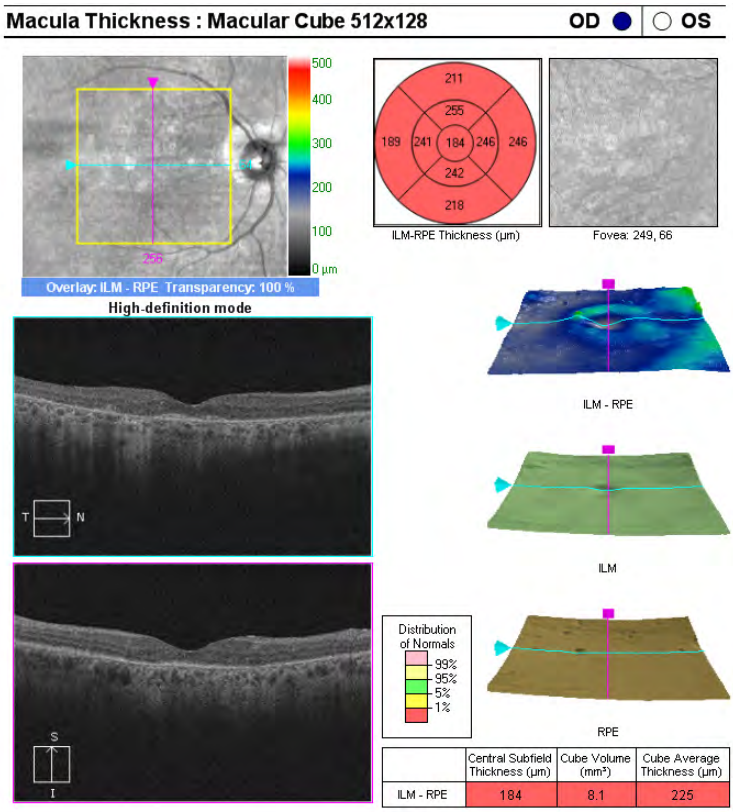
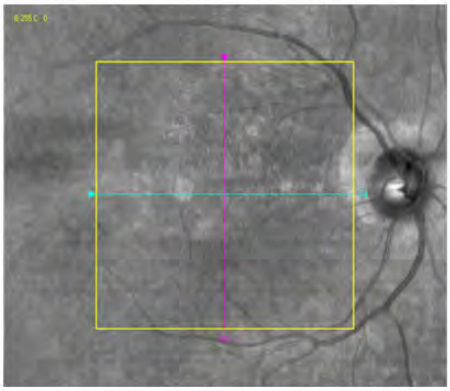
ADDUNDUM: 25 YEARS LATER …

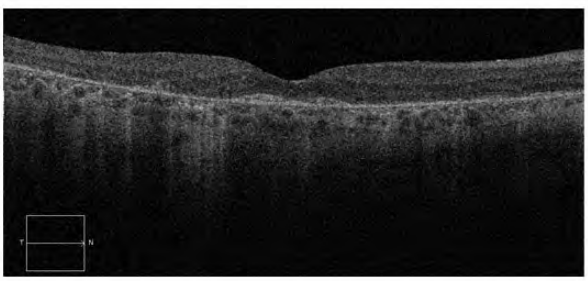
Case 7 Family B II9. Ophthalmoscopy: The flavimaculatus flecks have disappeared. Autofluorescence: Extension of the flavimaculatus lesions. In 2012 visual acuity is 20/25 OU. The OCT shows marked retinal thinning











Case 8 Family B II9 Autofluorescence: Extension of the flavimaculatus lesions and central areolar atrophy. In 2012 visual acuity is 20/40 RE and 20/125 LE.